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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/560,577	06/23/2006	Mark N. Bobrow	NEN-22302/16	8781

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EXAMINER	
HAQ, SHAFIQUL	
ART UNIT	**PAPER NUMBER**
1641	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/22/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/560,577	BOBROW, MARK N.	
	Examiner	Art Unit	
	Shafiqul Haq	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/15/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Information Disclosure Statement

1. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

4. Claim 1 recites the phrase "analyte-dependent enzyme activation system which reacts with a substrate portion of a conjugate" in lines 2-3. It is unclear what compounds are intended to encompass by the term "analyte-dependent enzyme activation system" that reacts with a substrate portion in the assay. The phrase "which activated conjugate covalently binds to a site on a surface having a receptor for said activated conjugate, said receptor not being reactive with the analyte-dependent enzyme activation system" is vague and indefinite because it is unclear what is intended to

encompass in this claim by the above phrase. First of all, the nature and structure of receptor that binds with the activated conjugate is unclear and its not clear whether enzyme-dependent enzyme activation system comprises a receptor for the activated conjugate. The phrase "said receptor not being reactive with the analyte-dependent enzyme activation system" does not exclude reaction of the activated conjugate with the analyte-dependent enzyme activation system.

5. Claim 10 recites the phrase "reacting the first product of step a) with an analyte-dependent enzyme activation system wherein the analyte-dependent enzyme activation is a member of a specific binding pair coupled to an enzyme , or is an enzyme, so as to produce a second product" in step b). It is not clear from claim language whether in step b), the analyte-dependent enzyme activation system specifically binds with the corresponding binding pair present in the analyte bound to solid phase i.e. the second product is unclear. It is also unclear as well as confusing as to what product is produced with the analyte when the analyte-dependent enzyme activation system is an enzyme because the enzyme is reacted in subsequent steps c) and d) with a substrate for the enzyme. Therefore, it is unclear the second product produced in step b) and thus unclear what is reacted with the enzyme substrate in step d) as in step d) it recites "reacting the second product of step b) with said enzyme substrate material". Step d) is vague and indefinite because of unclear nature of second product of step b). Step b) recites " activated conjugate which is a first member of a specific binding pair wherein the activated conjugate deposits covalently on the solid phase by binding to a second member of the specific binding pair on the

surface of solid phase". It is unclear how the binding of the activated first member of a specific binding pair is achieved with the second member of specific binding pair? Is it through specific binding member or through activated molecule produced by enzyme action on the first binding member because the term "deposits" does not imply specific binding though binding members. Applicants is advised to clearly write each step so that the steps are clear and particularly point out and distinctly claim the subject matter which applicant regards as the invention

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 15-17 and 20 are rejected under 35 U.S.C. 102(a) as being anticipated by Tsai et al. (American Chemical Society 2002).

Tsai et al. disclose a compound comprising a recognition head (Glucose) connected through a beta-glycosidic linkage to a p-hydroxy benzylic fluoride moiety, which is connected to a reporter (biotin) through a lnker. The recognition head (i.e. glucose) with ß-glucosidic linkage is a phosphorous free group and is capable is cleaved by a hydrolytic enzyme such as ß-glucosidase. The product as described in this reference anticipates at least one of the compounds disclosed in claim 15 of

instant application when in the compounds of claim 15, Y= a phosphorous free group capable of being cleaved by a hydrolytic enzyme, X= a group and L= a reporter. Therefore, the reference is deemed to anticipate the cited claims.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 1-4 and 6-14 are rejected under 35 U.S.C. 103(a) as being obvious over Babrow et al. (US 5,583,001) in view of Lo et al. (Journal of proteome Research 2002).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the

inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Bobrow et al. in a method for detection or quantitation of an analyte disclose using an analyte-dependent enzyme activation system which reacts with a substrate portion of a detectably labeled conjugate to form and activated conjugate that binds with a receptor on a surface, wherein the detectably labeled portion of the could conjugate are detected directly or indirectly. Bobrow et al. further disclose that the receptor do not react with the analyte-dependent enzyme activation system (see claims 1 and 13). Bobrow et al. disclose biotin tyramine, fluorescein tyramine or p-hydroxyphenylpropionyl-biocytin (see claim 7) as labeled substrate that is activated upon reaction with a enzyme, which then binds to nearby electron rich moieties such as tyrosine present in the proteins on solid support (column 7, lines 20-29). The immunoassay steps disclosed by Bobrow et al. is very similar to the assay method steps in claim 1 and 10 of instant application except that Bobrow fails to disclose labeled conjugate comprising parahydroxy benzylic halide moiety as disclosed in claims 1 and 10.

Lo et al. disclose a strategy for activity based detection of analyte (e.g. PTP-1B) in a sample. In the strategy described by Lo et al, analyte is allowed to react with a labeled conjugate comprising a recognition head (e.g. phenyl phosphate group), a

trapping device (derived from p-hydroxymandelic acid) and a reporter, which takes advantage of the quinine methide chemistry. The compound as described in this reference anticipates at least one of the compounds disclosed in claims 1 and 10 of instant application when in the compounds of claims 1 and 10, Y= a group capable of being cleaved by a hydrolytic enzyme, X= a group and L= a detectable label. Phosphatases (e.g. tyrosine phosphatase) present in the analyte remove phosphate group which leads to reactive quinine methide intermediate that in turn alkylate nearby electron rich nucleophiles on the biocatalyst resulting in the biocatalyst being labeled, which can then be detected directly or indirectly. Lo et al. further disclose that hydrolysis of the labeled conjugate by PTP-IB is specific rendering selective labeling of PTP-1B which provides a powerful tools in identifying new members of the important PTP family.

Therefore, considering the above fact that conjugate comprising parahydroxy benzylic halide moiety is useful as a conjugate with a label to selectively interact with receptor (e.g. PTP-1B family) upon activation with a enzyme, it would be obvious to one of Irdinary skill in the art at the time the invention was made to include labeled parahydroxy benzylic halide substrate of Lo et al. in the detection method of Bobrow et al. to efficiently detect new member of PTP families with a reasonable expectation of success.

As for kit claim 14, Bobrow et al. disclose amplification detection system in a kit (paragraph 13, lines 20-22) and the packaging of components in kit form is a well-known obvious expedient for ease and convenience in assay performance and once a

method has been established, one skilled in the art would clearly consider compiling in a kit format and change/modify different components of the kit to best suit the assay.

10. Claim 5 is are rejected under 35 U.S.C. 103(a) as being obvious over Babrow et al. (US 5,583,001) and Lo et al. (Journal of proteome Research 2002) as described above in the immediate preceding paragraph and further in view of Tsai et al. (American Chemical Society 2002).

See the above teaching of Babrow et al. and Lo et al.

Babrow et al. and Lo et al. differ from the instant application in failing to disclose glycosides as recognition head in the substrate conjugate.

Tsai et al. disclose a compound comprising a recognition head (Glucose) connected through a beta-glycosidic linkage to a p-hydroxy benzylic fluoride moiety, which is connected to a reporter (biotin) through a Inker. The recognition head is capable is cleaved by a hydrolytic enzyme such as ß-glucosidase. The compound as described in this reference anticipates at least one of the compounds disclosed in claims 1 and 10 of instant application when in the compounds of claims 1 and 10, Y= a group capable of being cleaved by a hydrolytic enzyme, X= a group and L= a detectable label. Enzymes present in the analyte remove beta-glycosidic linkage, which leads to reactive quinine methide intermediate that in turn alkylate nearby nucleophiles on the biocatalyst resulting in the enzyme to be labeled, which can then be detected directly or indirectly.

Tsai et al. disclose that the activity probes could serve in a wide range of applications depending on the property of the reporter gene and envisioned for rapid screening of glycosidases from numerous microbial sources. Tasi et al. further disclose various sugar units as well as large number of linker/reporter combination can be included in the conjugate compound to meet demands in various applications (page 3609, right column).

Therefore, considering the above fact that enzyme substrate conjugate having having beta glycosidic linkage can be used with enzyme activation system (Tsai et al.), it would be obvious to one of ordinary skill in the art at the time the invention was made to include labeled the labeled substrate of Tsai et al. in the detection method of Bobrow et al. to efficiently detect glycosidase with a reasonable expectation of success.

11. Claims 18-19 are rejected under 35 U.S.C. 103 (a) as being anticipated by Tsai et al. (American Chemical Society 2002) in view of Burton (US 2004/0235081A1).

As described above, Tsai et al. disclose a compound comprising a recognition head (Glucose) connected through a beta-glycosidic linkage to a p-hydroxy benzylic fluoride moiety, which is connected to a reporter (biotin) through a Inker. The recognition head is capable is cleaved by a hydrolytic enzyme such as ß-glucosidase. The compound as described in this reference anticipates at least one of the compounds disclosed in claims 1 and 10 of instant application when in the compounds of claims 1 and 10, Y= a group capable of being cleaved by a hydrolytic enzyme, X= a group and L= a detectable label. Enzymes present in the analyte

remove beta-glycosidic linkage, which leads to reactive quinine methide intermediate that in turn alkylate nearby nucleophiles on the biocatalyst resulting in the enzyme to be labeled, which can then be detected directly or indirectly.

Tsai et al. disclose that the activity probes could serve in a wide range of applications depending on the property of the reporter groups. Tasi et al. further disclose various sugar units as well as large number of linker/reporter combination can be included in the conjugate compound to meet demands in various applications (page 3609, right column).

Tsai et al., however, fail to disclose other linkages beside glycosidic linkage for detection of enzymatic activities.

Burton discloses a method for detection of enzyme activity requiring an enzyme substrate comprising detectable compound conjugated to an enzyme cleavable group attached via an ester or ether linkage to oxygen atom derived from a hydroxyl group of the detectable compound (see abstract). Button discloses that a wide variety of enzyme cleavable groups and bonds (linkages e.g. ester linkages, sulphonate or sulfate ester linkages, glycosidic linkages) may be used in the enzyme substrate depending on the enzyme studied (paragraph [0028]).

Therefore, one of ordinary skill in the art at the time the invention was made could readily envisioned other reporter substrate having other linkages (e.g. ester linkage) in the compound of Tsai et al. for detection of other enzymes specific for other linkages.

Double Patenting

12. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

13. Claims 1-4 and 6-14 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-24 of U.S. Patent No. 5,583,001 in view of Lo et al. (Journal of proteome Research 2002).

Bobrow et al. in the Patent of 001' disclose a method for detection or quantitation of an analyte disclose using an analyte-dependent enzyme activation system which reacts with a substrate portion of a detectably labeled conjugate to form and activated conjugate that binds with a receptor on a surface, wherein the detectably labeled portion of the could conjugate are detected directly or indirectly. Bobrow et al. further disclose that the receptor do not react with the analyte-dependent enzyme activation

system (see claims 1 and 13). Bobrow et al. disclose biotin tyramine, fluorescein tyramine or p-hydroxyphenylpropionyl-biocytin (see claim 7) as labeled substrate that is activated upon reaction with a enzyme, which then binds to nearby electron rich moieties such as tyrosine present in the proteins on solid support (column 7, lines 20-29). The immunoassay steps disclosed by Bobrow et al. is very similar to the assay method steps in claim 1 and 10 of instant application except that Bobrow fails to disclose labeled conjugate comprising parahydroxy benzylic halide moiety as disclosed in claims 1 and 10.

Lo et al. disclose a strategy for activity based detection of analyte (e.g. PTP-1B) in a sample. In the strategy described by Lo et al, analyte is allowed to react with a labeled conjugate comprising a recognition head (e.g. phenyl phosphate group), a trapping device (derived from p-hydroxymandelic acid) and a reporter, which takes advantage of the quinine methide chemistry. The compound as described in this reference anticipates at least one of the compounds disclosed in claims 1 and 10 of instant application when in the compounds of claims 1 and 10, Y= a group capable of being cleaved by a hydrolytic enzyme, X= a group and L= a detectable label. Phosphatases (e.g. tyrosine phosphatase) present in the analyte remove phosphate group which leads to reactive quinine methide intermediate that in turn alkylate nearby electron rich nucleophiles on the biocatalyst resulting in the biocatalyst being labeled, which can then be detected directly or indirectly. Lo et al. further disclose that hydrolysis of the labeled conjugate by PTP-IB is specific rendering selective labeling

of PTP-1B which provides a powerful tools in identifying new members of the important PTP family.

Therefore, considering the above fact that conjugate comprising parahydroxy benzylic halide moiety is useful as a conjugate with a label to selectively interact with receptor (e.g. PTP-1B family) upon activation with a enzyme, it would be obvious to one of Irdinary skill in the art at the time the invention was made to include labeled parahydroxy benzylic halide substrate of Lo et al. in the detection method of 001' patent to efficiently detect new member of PTP families with a reasonable expectation of success.

As for kit claim 14, Bobrow et al. disclose amplification detection system in a kit (paragraph 13, lines 20-22) and the packaging of components in kit form is a well-known obvious expedient for ease and convenience in assay performance and once a method has been established, one skilled in the art would clearly consider compiling in a kit format and change/modify different components of the kit to best suit the assay.

14. Claim 5 is rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-24 of U.S. Patent No. 5,583,001 in view of Lo et al. (Journal of proteome Research 2002). and further in view of Tsai et al. (American Chemical Society 2002).

See the above teaching of Babrow et al. and Lo et al.

US paten 5,853,001 (Babrow et al.) and Lo et al. differ from the instant application in failing to disclose glycosides as recognition head in the substrate conjugate.

Tsai et al. disclose a compound comprising a recognition head (Glucose) connected through a beta-glycosidic linkage to a p-hydroxy benzylic fluoride moiety, which is connected to a reporter (biotin) through a lnker. The recognition head is capable is cleaved by a hydrolytic enzyme such as ß-glucosidase. The compound as described in this reference anticipates at least one of the compounds disclosed in claims 1 and 10 of instant application when in the compounds of claims 1 and 10, Y= a group capable of being cleaved by a hydrolytic enzyme, X= a group and L= a detectable label. Enzymes present in the analyte remove beta-glycosidic linkage, which leads to reactive quinine methide intermediate that in turn alkylate nearby nucleophiles on the biocatalyst resulting in the enzyme to be labeled, which can then be detected directly or indirectly.

Tsai et al. disclose that the activity probes could serve in a wide range of applications depending on the property of the reporter gene and envisioned for rapid screening of glycosidases from numerous microbial sources. Tasi et al. further disclose various sugar units as well as large number of linker/reporter combination can be included in the conjugate compound to meet demands in various applications (page 3609, right column).

Therefore, considering the above fact that enzyme substrate conjugate having having beta glycosidic linkage can be used with enzyme activation system (Tsai et

al.), it would be obvious to one of ordinary skill in the art at the time the invention was made to include labeled the labeled substrate of Tsai et al. in the detection method of of 011' patent to efficiently detect glycosidase with a reasonable expectation of success.

Conclusion

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shafiqul Haq whose telephone number is 571-272-6103. The examiner can normally be reached on 7:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SHAFIQUL HAQ
EXAMINER
ART UNIT 1641

LONG V. LE 04/16/07
SUPERVISORY PATENT EXAMINER
ART UNIT 1641